3×600 mg capsules of unlabelled resin three times a day for 28 days (total daily dose=5400 mg). Sixteen subjects are admitted to the clinical research metabolic unit at a designated center, to continue with the radiolabel portion of the study. On the morning of the first confinement day, the subjects receive a single oral 2.4 g dose (4×600 mg capsules) of 14C-labelled resin for a total of 480 uCi of 14C per subject. Unlabelled resin is then administered as before over the next three days. Blood samples are drawn at 0, 4, 8, 12, 24, 48, 72, and 96 hours. Voided urine and feces are collected at baseline over the intervals 0-24 hr, 24-48 hr, 48-72 hr, 72-96 hr. Homogenized fecal and whole blood samples are dried and oxidized prior to scintillation counting. Radioactivity in the blood, urine, and feces is expressed as a percentage of the administered dose for each time interval and as a total percentage. Properties of a non-absorbed resin are: (i) no detectable amounts of 14C-resin in the whole blood of any subject at any time during the study; (ii) for each subject, <0.009% of the labeled-resin dose in the collected urine samples, covering the 96 hour period following administration of the labeled-resin; and (iii) for each subject, >99% of the dose is recovered in the feces over a 10 day period following 14C-resin administration.

Example 6

Animal Models to Demonstrate Na-Binding Capacity of Resins

Animal models are used to demonstrate the binding of sodium cations by the resins, which are supplemented into a controlled diet administered to rats or dogs. These studies generally are conducted in normal animals to demonstrate an effect of the resin, then in diseased animal models where a sustained imbalance of electrolytes leading to extravascular edema is created by compromising the kidney, liver, or cardiac function of the test animal.

A typical experiment with normal rats to determine relative binding efficiency of the test polymers uses three groups (n=6/group) of Sprague-Dawley female rats placed in single metabolic cages on a diet consisting of low-sodium biscuits and distilled water. Sodium is administered daily via oral feeding tube in three doses as a 200 mM solution (2.4 mEq). During the first three days of the test, baseline data are collected in the form of mEq/day of sodium in the urine and mEq/day of sodium in feces; usual sodium measures are 2.25-2.5 mEq/day in urine and 0.05-0.3 mEq/day in feces. In the next three days, the three groups of test animals receive fixed doses of the test resin (500, 1000, 2000 mg/kg/d) in addition to the saline solution administered by oral gavage over three doses. In the final three days of the test, the resin is removed from the oral gavage and saline solution is administered as in the first period to provide a second, follow-up control period. Active resins are those that decrease sodium in the urine during the second dosing period below 2.25 mEq/day (typical ranges are 0.25-1.5 mEq/day) and increase the sodium content of the feces (typical values range from 2 mEq/g-5 mEq/g of resin). Sodium content in urine and feces is determined by extraction and ion exchange chromatography or by flame photometry.

A typical experiment with rats that have compromised kidney function, used to mimic hypertension and fluid retention in the ESRD patient, uses chemical induction of kidney damage (uranyl acetate, gentamicin, cephaloradine, etc) or surgical resection of the kidney (⅝ths nephrectomy) to induce chronic renal failure. After the chemical or surgical manipulation of the animals and stabilization of renal function at a reduced state, the animals are divided into three test groups (n=10/group). As in the normal animal tests, the test animals are maintained for 3 days on low-sodium biscuits and receive 75 mM NaCl solution ad lib; baseline sodium values are determined for urine and feces. The animals in each group are then given fixed amounts of the resin by oral gavage (3 doses, total daily doses of 500, 1000, and 2000 mg/kg/d) for three days, with a "washout" period for three days following resin dosing. Sodium in urine and feces is determined throughout the baseline, test and washout periods; sodium content in the urine is generally elevated in the baseline and washout periods (4-5 mEq/d), but is reduced in the treatment phase (1-2 mEq/d). Similarly, fecal sodium in the baseline and washout groups is 0.03-0.5 mEq/d and increases to 3.8-5 mEq/g of resin in the treated animals.

Example 7

Human Volunteer Studies to Demonstrate Sodium-Binding Capacity of Resins

Completion of IND-enabling safety pharmacology and toxicology analysis of the resins will allow human volunteer studies in normal subjects, to evaluate the in vivo binding capacity of the test resins. The design of a typical study enrolls 24 normal subjects housed in a clinical metabolic unit; the subjects have normal body weight, hematology and chemistry tests and have no history of GI, renal or hepatic disease. After screening, the volunteers are randomized into 3 groups of 8 subjects each; six of the subjects in each group are randomized to receive a specific dose of resin (25 mg/kg; 70 mg/kg; 140 mg/kg) and two receive placebo. The volunteers are housed on the metabolic unit for 18 days and consume a sodium-controlled diet of 5 g elemental sodium per day (3 meals plus 1 snack). The study design is as follows; on day 1, the subjects receive a single oral dose of resin or placebo according to treatment group. For the next seven days (d2-d8) the subjects receive no drug; from the morning of day 5 to the morning of day 9, 24 hr urine and feces are collected and the sodium and potassium content of the samples determined. On days 9-16, all subjects receive the same dosing according to group, with the doses divided over three daily doses; total urine and feces are collected from day 13 through day 17. The subjects are discharged on day 18. Fecal sodium content is elevated in the treatment groups, approaching 4-5 mEq/g resin.

All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

It will be apparent to one of ordinary skill in the art that many changes and modifications can be made thereto without departing from the spirit or scope of the appended claims.

The invention claimed is:

1. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a cation exchange, crosslinked alpha-fluoroacrylic acid polymer or a salt thereof, wherein the alpha-fluoroacrylic acid polymer is crosslinked with divinylbenzene and is in bead form.

2. The pharmaceutical composition of claim **1** suitable for oral or intestinal administration.

3. The pharmaceutical composition of claim **2** suitable for oral administration.

4. The pharmaceutical composition of claim **2** suitable for intestinal administration.